

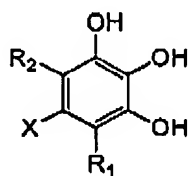
Application S. No. 10/762,444

Filed: January, 21, 2004

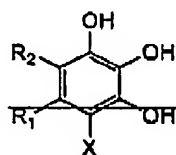
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Listing of claims:

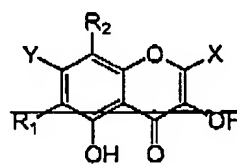
1. (Currently amended) A drug product for the treatment of amyloidosis in a mammal suffering therefrom, comprising a container labeled or accompanied by a label indicating that the drug product is for the treatment of amyloidosis, the container containing one or more dosage units each comprising at least one pharmaceutically acceptable excipient and, as an active ingredient, an isolated pure compound selected from the group consisting of the compounds of formula A, formula B, formula C, formula D, and formula E:



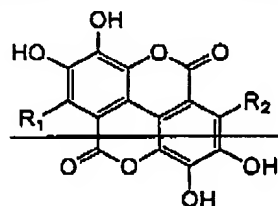
Formula A



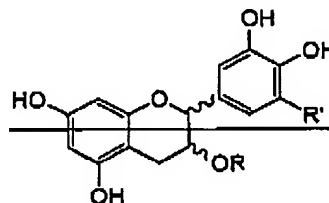
Formula B



Formula C



Formula D



Formula E

where:

~~R is selected from the group consisting of hydrogen, 2,3-dihydroxybenzoyl, 3,4-dihydroxybenzoyl, 2,3,4-trihydroxybenzoyl, and 3,4,5-trihydroxybenzoyl;~~

~~R' is hydrogen or OH; R₁ and R₂ are independently selected from hydrogen, halogen, C₁₋₆ alkyl and C₁₋₆ alkoxy, each alkyl and alkoxy group optionally substituted with up to 5 halogen atoms and non-interfering substituents;~~

X is selected from hydrogen and the group consisting of

(a) hydroxy, amino, C₁₋₆ alkylamino, di(C₁₋₆ alkyl)amino, and cycloamino,

(b) C₁₋₂₂ alkyl, C₁₋₂₂ alkoxy, C₁₋₂₂ alkylthio, and C₁₋₂₂ alkylcarboxyl, each optionally substituted with 1 to 5 moieties selected from the group consisting of halogen, hydroxy, mercapto, amino, nitro, C₁₋₆ alkoxy, C₁₋₆ alkylthio, and C₁₋₆ alkylcarboxyl,

(c) aromatic and heteroaromatic groups substituted with 2 or 3 adjacent hydroxy groups, and optionally substituted with 1 to 5 non-interfering substituents,

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(d) sugars, optionally substituted with one or more anionic groups selected from sulfate, phosphate, phosphonate, carboxylate, and sulfonate groups, and

(e) peptides and peptide derivatives, and

(f) ~~C(O)R₃ and C(O)OR₃, where R₃ is selected from the group consisting of (a) through (e) above; and Y is hydrogen, hydroxy, C₁₋₆ alkoxy, benzyloxy, where the phenyl group is optionally substituted with 1 to 3 substituents selected from halo and C₁₋₆ alkyl, or -OSO₂R₄, where R₄ is C₁₋₆ alkyl or phenyl optionally substituted with 1 to 3 substituents selected from halo and C₁₋₆ alkyl; and~~

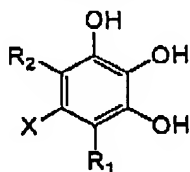
~~the group of compounds consisting of acacetin, actinorhodine, alizarin, alizarin blue, alizarin orange, alizarinsulfonic acid, alkannin, anthragallol, anthralin, anthrarobin, anthrarufin, apigenin, apigetrin, apiose, baicalein, baptigenin, 1,2,4-benzenetriol, bostrycoidin, carbidopa, carminic acid, carubicin, cellobiose, centaurein, chloranilic acid, chondrosine, chromotrope 2B, chromotropic acid, chrysamminic acid, chrysarobin, chrysin, chrysophanic acid, eichlorin, citrazinic acid, citromycetin, collinomyein, curvularin, cyanidin, cyanidin 3-glucoside, cyanidin 3-rhamnoglucoside, cyanidin 3,5-diglucoside, cyanidin 3-sophoroside, daphnetin, datiscetin, daunorubicin, delphinidin, deoxyepinephrine, diosmetin, diosmin, dioxethedrine, dopa, dopamine, dextrorubicin, droxidopa, echinchrome A, embelin, emodin, ergoflavin, eriodictyol, esculetin, fenoldopam, fomecin A, fomecin B, fraxetin, fraxin, fredericamyein A, fumigatin, fusarubin, fuscic acid, fustin, galangin, gallein, galloyl, gardenin A, gardenin B, gardenin C, gardenin D, gardenin E, genistein, gentisin, granaticin, guamecycline, hematein, hydroxyphenyl, hydroxyphenyl, icariin, isochlorogenic acid, kaempferol, kermesic acid, laeaeic acid A, laeaeic acid B, laeaeic acid C, laeaeic acid D, leucoanthracidin, luteolin, maelurin, menogaril, methylated gallic acid, morin, oosporein, phenicin, phloroglucinol, puberulic acid, puberulonic acid, purpurin, purpurogallin, quercetin, quercetin, quinalizarin, quinic acid, resistomyein, rhamnetin, rhein, rhodizonic acid, rhodomyein A, rhodomyein B, robinin, ruberythric acid, rufigallol, rutin, scutellarein, tannic acid, tetroquinone, tiron, trolox, and tunichrome B1, but excluding pyrogallol, and the pharmaceutically acceptable salts thereof.~~

2. (Original) The drug product of claim 1 containing only one active ingredient compound.

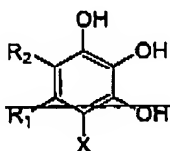
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3. (Original) The drug product of claim 2, wherein the label indicates that the drug product is for the treatment of Alzheimer's disease.

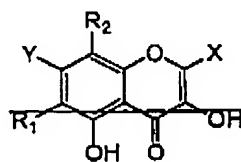
4. (Currently amended) A method of treating a mammal suffering from a Lewy body disease or Parkinson's disease characterized by α -synuclein fibril formation, comprising administration to the mammal of a therapeutically effective amount of an isolated pure compound selected from the group consisting of the compounds of formula A, ~~formula B, formula C, formula D, and formula E:~~



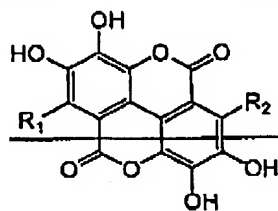
Formula A



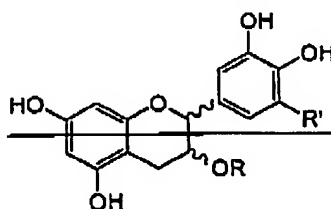
Formula B



Formula C



Formula D



Formula E

where:

~~R is selected from the group consisting of hydrogen, 2,3-dihydroxybenzoyl, 3,4-dihydroxybenzoyl, 2,3,4-trihydroxybenzoyl, and 3,4,5-trihydroxybenzoyl;~~

~~R' is hydrogen or OH; R1 and R2 are independently selected from hydrogen, halogen, C1-6 alkyl and C1-6 alkoxy, each alkyl and alkoxy group optionally substituted with up to 5 halogen atoms and non-interfering substituents;~~

X is selected from hydrogen and the group consisting of

(a) hydroxy, amino, C1-6 alkylamino, di(C1-6 alkyl)amino, and cycloamino,

(b) C1-22 alkyl, C1-22 alkoxy, C1-22 alkylthio, and C1-22 alkylcarboxyl, each optionally substituted with 1 to 5 moieties selected from the group consisting of halogen, hydroxy, mercapto, amino, nitro, C1-6 alkoxy, C1-6 alkylthio, and C1-6 alkylcarboxyl,

(c) aromatic and heteroaromatic groups substituted with 2 or 3 adjacent hydroxy groups, and optionally substituted with 1 to 5 non-interfering substituents,

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(d) sugars, optionally substituted with one or more anionic groups selected from sulfate, phosphate, phosphonate, carboxylate, and sulfonate groups, and

(e) peptides and peptide derivatives, and

~~(f) $C(O)R_3$ and $C(O)OR_3$, where R_3 is selected from the group consisting of (a) through (e) above; and Y is hydrogen, hydroxy, C_{1-6} -alkoxy, benzyloxy, where the phenyl group is optionally substituted with 1 to 3 substituents selected from halo and C_{1-6} -alkyl, or OSO_2R_4 , where R_4 is C_{1-6} -alkyl or phenyl optionally substituted with 1 to 3 substituents selected from halo and C_{1-6} -alkyl; and~~

~~the group of compounds consisting of acacetin, actinorhodin, alizarin, alizarin blue, alizarin orange, alizarinsulfonic acid, alkannin, anthragallol, anthralin, anthrarobin, anthrarin, apigenin, apigetrin, apiose, baicalein, baptigenin, 1,2,4-benzenetriol, bostrycoidin, carbidopa, carminic acid, carubicin, cellobiose, centaurein, chloranilic acid, chondrosine, chromotrope 2B, chromotropic acid, chrysaminic acid, chrysarobin, chrysin, chrysophanic acid, eichlerin, citrazinic acid, citromycin, collinomyces, curvularin, cyanidin, cyanidin 3-glucoside, cyanidin 3-rhamnoglucoside, cyanidin 3,5-diglucoside, cyanidin 3-sophoroside, daphnerin, datiscetin, daunerubicin, delphinidin, deoxyepinephrine, diosmetin, diosmin, dioxethedrine, dopa, dopamine, doxorubicin, droxidopa, echinochrome A, embelin, emodin, ergoflavin, eriodictyol, esouletin, fenoldopam, fomesin A, fomesin B, fraxetin, fraxin, fredericamycin A, fumigatin, fusarubin, fucosin, fustin, galangin, gallein, galloeyanin, gardenin A, gardenin B, gardenin C, gardenin D, gardenin E, genistein, gentisin, granatoin, guamecyclin, hematein, hydroxyspherobioside, hydroxysphoricoside, isariin, isochlorogenic acid, kaempferol, kermesic acid, laccase acid A, laccase acid B, laccase acid C, laccase acid D, leucoanthocyanidin, luteolin, maelurin, monogallin, methylenedigallin, morin, oesporin, phenolic, phloroglucinol, puberulic acid, puberulonic acid, purpurin, purpurogallin, quercetin, quercitrin, quinalizarin, quinic acid, resistanin, rhamnetin, rhein, rhodizonic acid, rhodomycin A, rhodomycin B, robinin, ruberythric acid, rufigallol, rutin, scutellarein, tannic acid, tetraquinone, tiron, trolox, and tunichrome B1, but excluding pyrogallol, and the pharmaceutically acceptable salts thereof.~~

5. (Original) The method of claim 4 where only one such compound is administered.

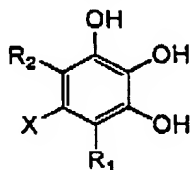
6. (Original) The method of claim 5 where the mammal is a human.

7. (Cancelled).

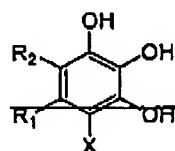
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8. (Currently amended) The method of ~~claim 7~~ claim 1, where the disease is Parkinson's disease.

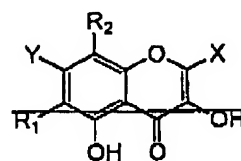
9. (Currently amended) A drug product for the treatment of a Lewy body disease or Parkinson's disease characterized by α -synuclein fibril formation in a mammal suffering therefrom, comprising a container labeled or accompanied by a label indicating that the drug product is for the treatment of a Lewy body disease or Parkinson's disease characterized by α -synuclein fibril formation, the container containing one or more dosage units each comprising at least one pharmaceutically acceptable excipient and, as an active ingredient, an isolated pure compound ~~selected from the group consisting of the compounds of formula A, formula B, formula C, formula D, and formula E:~~



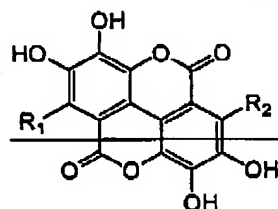
Formula A



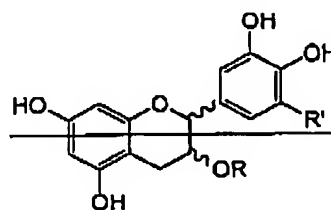
Formula B



Formula C



Formula D



Formula E

where:

~~R is selected from the group consisting of hydrogen, 2,3-dihydroxybenzoyl, 3,4-dihydroxybenzoyl, 2,3,4-trihydroxybenzoyl, and 3,4,5-trihydroxybenzoyl;~~

~~R' is hydrogen or OH; R1 and R2 are independently selected from hydrogen, halogen, C1-6 alkyl and C1-6 alkoxy, each alkyl and alkoxy group optionally substituted with up to 5 halogen atoms and non-interfering substituents;~~

X is selected from hydrogen and the group consisting of

(a) hydroxy, amino, C1-6 alkylamino, di(C1-6 alkyl)amino, and cycloamino,

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(b) C₁₋₂₂ alkyl, C₁₋₂₂ alkoxy, C₁₋₂₂ alkylthio, and C₁₋₂₂ alkylcarboxyl, each optionally substituted with 1 to 5 moieties selected from the group consisting of halogen, hydroxy, mercapto, amino, nitro, C₁₋₆ alkoxy, C₁₋₆ alkylthio, and C₁₋₆ alkylcarboxyl,

(c) aromatic and heteroaromatic groups substituted with 2 or 3 adjacent hydroxy groups, and optionally substituted with 1 to 5 non-interfering substituents,

(d) sugars, optionally substituted with one or more anionic groups selected from sulfate, phosphate, phosphonate, carboxylate, and sulfonate groups, and

(e) peptides and peptide derivatives, and

~~— (f) C(O)R₃ and C(O)OR₃, where R₃ is selected from the group consisting of (a) through (e) above; and Y is hydrogen, hydroxy, C₁₋₆ alkoxy, benzyloxy, where the phenyl group is optionally substituted with 1 to 3 substituents selected from halo and C₁₋₆ alkyl, or OSO₂R₄, where R₄ is C₁₋₆ alkyl or phenyl optionally substituted with 1 to 3 substituents selected from halo and C₁₋₆ alkyl; and~~

~~— the group of compounds consisting of acacetin, actinorhodine, alizarin, alizarin blue, alizarin orange, alizarinsulfonic acid, alkanin, anthracolol, anthralin, anthrarobin, anthraquin, apigenin, apigenin, apiose, baicalin, baptigenin, 1,2,4-benzenetriol, bostrycoidin, carbidopa, carminic acid, carubicin, cellobiose, centaurein, chloranilic acid, chondresine, chromotrope 2B, chromotropic acid, chrysaminic acid, chrysarobin, chrysin, chrysophanic acid, eichlerin, citrazinic acid, citromycin, collinomydin, curvularin, cyanidin, cyanidin 3-glucoside, cyanidin 3-rhamnoglucoside, cyanidin 3,5-diglucoside, cyanidin 3-sophoroside, daphnetin, datiscetin, daurorubicin, delphinidin, deoxyepinephrine, diosmetin, diosmin, dioxethedrine, dopa, dopamine, dextrorubicin, droxidopa, echinochrome A, embelin, emodin, ergoflavin, eriodictyol, esculetin, fenoldopam, fomesin A, fomesin B, fraxetin, fraxin, fredericamycin A, fumigatin, fusarubin, fucsin, fustin, galangin, gallein, gallocyanine, gardenin A, gardenin B, gardenin C, gardenin D, gardenin E, genistein, gentisin, granatoin, guameocycline, hematoin, hydroxysphorobioside, hydroxysphoricoside, icariin, isoquercitrin, kaempferol, kermesic acid, laccic acid A, laccic acid B, laccic acid C, laccic acid D, leucoeyanidin, luteolin, maelurin, menogaril, methylenedigallie acid, morin, oosperein, phenicin, phloroglucide, puberulic acid, puberulonic acid, purpurin, purpureogallin, quercetogenin, quercitrin, quinalizarin, quinic acid, resistomydin, rhamnetin, rhein, rhodizonic acid, rhodomycin A, rhodomycin B, robinin,~~

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~~ruberythric acid, rufigallol, rutin, scutellarein, tannic acid, tetraquinone, tiron, trolox, and
tunicic acid~~, but excluding pyrogallol, and the pharmaceutically acceptable salts thereof.

10. (Original) The drug product of claim 9 containing only one such compound.

11. (Original) The drug product of claim 10 indicated for the treatment of Parkinson's disease.